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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/074,472	05/07/1998	MARK M. RICHTER	337462000600	2284

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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/04/2002 34

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/074,472	Richter et al
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- ***The MAILING DATE of this communication appears on the cover sheet with the correspondence address*** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.*
- *If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.*
- *If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.*
- *Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).*
- *Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).*

Status

1) ☒ *Responsive to communication(s) filed on Oct 18, 2002 .*

2a) ☒ *This action is* **FINAL.** 2b) ☐ *This action is non-final.*

3) ☐ *Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.*

Disposition of Claims

4) ☒ *Claim(s) 30-33 is/are pending in the application.*

4a) *Of the above, claim(s) _____ is/are withdrawn from consideration.*

5) ☐ *Claim(s) _____ is/are allowed.*

6) ☒ *Claim(s) 30-33 is/are rejected.*

7) ☐ *Claim(s) _____ is/are objected to.*

8) ☐ *Claims _____ are subject to restriction and/or election requirement.*

Application Papers

9) ☐ *The specification is objected to by the Examiner.*

10) ☐ *The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.*

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ *The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.*

If approved, corrected drawings are required in reply to this Office action.

12) ☐ *The oath or declaration is objected to by the Examiner.*

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ *Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).*

a) ☐ *All* b) ☐ *Some** c) ☐ *None of:*

1. ☐ *Certified copies of the priority documents have been received.*
2. ☐ *Certified copies of the priority documents have been received in Application No. _____ .*
3. ☐ *Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).*

**See the attached detailed Office action for a list of the certified copies not received.*

14) ☐ *Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).*

a) ☐ *The translation of the foreign language provisional application has been received.*

15) ☐ *Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.*

Attachment(s)

1) ☐ *Notice of References Cited (PTO-892)*
2) ☐ *Notice of Draftsperson's Patent Drawing Review (PTO-948)*
3) ☐ *Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____*
4) ☐ *Interview Summary (PTO-413) Paper No(s). _____*
5) ☐ *Notice of Informal Patent Application (PTO-152)*
6) ☐ *Other:*

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 30-31 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Talley et al. (U.S. Patent 6,132,955) (October 17, 2000) in view of Haugland et al. (U.S. Patent 5,798,276) (August 25, 1998) further in view of Carrico (U.S. Patent 4,743,535) (May 10, 1988).

Talley et al. teach a method for quantitative electrochemiluminescence detection of an oligonucleotide target analyte in a sample (abstract and Column 12, lines 45-49), the method comprising the steps of:

(a) preparing an assay mixture comprising: the sample, (Abstract);

one or more assay reagents comprising a labeled complex comprising an ECL label selected from ruthenium bipyridine complexes and osmium bipyridine complexes attached to an oligonucleotide probe complementary to the analyte and capable of hybridizing therewith, the label capable of generating a detectable ECL emission, wherein the labeled complex is immobilized on a magnetic particle (Column 10, lines 38-67 and Column 5, lines 56-60 and Examples 1-3); and

a coreactant (Examples 1-3)

b) bringing the assay mixture into contact with a working electrode (Column 3, lines 40-43 and Examples 1-3);

c) applying a potential to the electrode, thereby enabling an ECL reaction to proceed (Example 1 and Claim 1);

d) separating unhybridized labeled complex from hybridized complex (Column 5, lines 55-60 and Column 6, lines 4-32);

e) measuring the ECL emission produced by the label hybridized to the analyte via the oligonucleotide probe (Examples 1-3 and Claim 1), and

f) correlating the measured ECL emission with the amount of the analyte in the sample (Examples 1-3 and Claim 1).

Talley et al do not teach a method wherein the reagent comprises at least one moiety selected from the group consisting of phenol and benzoquinone.

Haugland et al. teach the method wherein the reagent comprises at least one moiety selected from the group consisting of phenol and benzoquinone (Column 2, line 52 to column 3, line 15).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to include the group of chemicals containing phenol of Haugland et al. in the method of Talley et al., since Haugland et al. state, "Dyes that are able to preferentially bind to a specific biological ingredient in a sample enable the researcher to determine the presence or quantity of that specific ingredient. In addition, specific cellular structures can be monitored with respect to their spatial and temporal distribution in diverse environments. Many applications utilize chemically reactive fluorescent dyes by chemically attaching the dye to reactive sites on a wide variety of materials such as cells, tissues, proteins, antibodies, enzymes, drugs, hormones, lipids, nucleotides, nucleic acids, or natural or synthetic polymers to make fluorescent conjugates (Column 1, lines 15-27)." An ordinary practitioner would have been motivated to combine and compare the electrochemiluminescence quenching chemicals containing deferentially substituted phenol ring of Haugland et al. into the method of Talley et al. in order to achieve the express advantages, as noted by Haugland et al., of dyes, that are able to preferentially bind to a specific

biological ingredient in a sample, which enables the researcher to determine the presence or quantity of that specific ingredient and in addition, to monitor specific cellular structures with respect to their spatial and temporal distribution in diverse environments and in addition has many applications that utilize chemically reactive fluorescent dyes by chemically attaching the dye to reactive sites on a wide variety of materials such as cells, tissues, proteins, antibodies, enzymes, drugs, hormones, lipids, nucleotides, nucleic acids, or natural or synthetic polymers to make fluorescent conjugates.

Talley et al in view of Haugland et al do not teach the combination of dyes containing ECL quenching moiety and ECL inducing moiety.

Carrico teaches the combination of dyes containing ECL quenching moiety and ECL inducing moiety (Column 2, lines 34-54).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the combination of dyes containing ECL quenching moiety and ECL inducing moiety of Carrico in the method of Haugland et al. in view of Talley et al., since Carrico states, "It is proposed to employ a pair of probes which hybridize to contiguous regions on a polynucleotide sequence of interest and to label one probe with a chemiluminescent catalyst such as the enzyme peroxidase and the other with an absorber molecule for the chemiluminescent emission. The catalyst and absorber labels must be situated near the contiguous terminal ends of the respective probes such that upon hybridization there is observed quenching of the chemiluminescent emission by energy transfer to the absorber

molecule (Column 2, lines 37-47)." An ordinary practitioner would have been motivated to combine and substitute the combination of dyes containing ECL quenching moiety and ECL inducing moiety of Carrico in the method of Haugland et al. in view of Talley et al., in order to achieve the express advantages, as noted by Carrico, of a method which provides probes such that upon hybridization there is observed quenching of the chemiluminescent emission by energy transfer to the absorber molecule.

3. Claims 30-33 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Talley et al. (U.S. Patent 6,132,955) (October 17, 2000) in view of Haugland et al. (U.S. Patent 5,798,276) (August 25, 1998) further in view of Carrico (U.S. Patent 4,743,535) (May 10, 1988) further in view of Stratagene Catalog (1988, Page 39).

Talley et al. in view of Haugland et al. further in view of Carrico expressly teach the method claims and assay reagents of claims 30-31 as described above in detail.

Talley et al. in view of Haugland et al. further in view of Carrico do not teach the motivation to combine all the reagents for detecting an analyte in a sample in the form of a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a suitable container, ECL label and ECL quenching moiety of Talley et al. in view of Haugland et al. further in view of Carrico into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have

been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control (page 39, column 1).

Response to Arguments

4. Applicant's arguments filed on October 18, 2002 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Haugland et al. since Haugland et al. state, "Dyes that are able to preferentially bind to a specific biological ingredient in a sample enable the researcher

to determine the presence or quantity of that specific ingredient. In addition, specific cellular structures can be monitored with respect to their spatial and temporal distribution in diverse environments. Many applications utilize chemically reactive fluorescent dyes by chemically attaching the dye to reactive sites on a wide variety of materials such as cells, tissues, proteins, antibodies, enzymes, drugs, hormones, lipids, nucleotides, nucleic acids, or natural or synthetic polymers to make fluorescent conjugates (Column 1, lines 15-27)." The same logic is applicable to other combinatory references as well.

Applicant then argues the 103 rejection is improper because it lacks a reasonable expectation of success.

With regard to the "lacks a reasonable expectation of success." argument, The MPEP 2143.02 states, "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart , 531 F.2d 1048, 189 USPQ 143 (CCPA 1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also Amgen, Inc. v. Chugai

Pharmaceutical Co ., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied , 502 U.S. 856 (1991) (In the context of a biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); In re O'Farrell , 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.)."

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Carrico reference of the enabling methodology, the suggestion to modify the prior art, and evidence that a number of different combination of dyes containing chemiluminescence quenching moiety and chemiluminescence inducing moiety were actually experimentally studied and found to be functional (Examples I-III). This evidence of functionality trumps the attorney arguments, which argues that Carrico reference is an invitation to research, since Carrico steps beyond research and shows the functional product.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

October 31, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600